REMARKS

Claims 1-3, 7, 8, 10-12, and 14 are currently pending. Claim 14 is withdrawn from consideration pursuant to a Restriction Requirement. Claims 1-3, 7, and 8 are rejected under 35 U.S.C. § 102(b) and claims 1-3, 7, 8, 10-12 are rejected under 35 U.S.C. § 103(a). These rejections are addressed as follows.

Rejection under 35 U.S.C. § 102(b)

Claims 1-3, 7, and 8 are rejected as being anticipated by Fodor (U.S. Patent Application No. 2001/0053519). The Examiner states "Fodor teaches an array comprising all possible nucleic acid sequences of any given length. For example a 10-mer array comprises all possible oligonucleotides containing 10 base positions (Col 17, lines 23-36). While Fodor does not specifically discuss probes for detecting [the claimed] point mutations . . .it is a property of the array taught by Fodor that it would comprise probes capable of detecting these point mutations." Thus, the Examiner concludes that the genus described by Fodor (e.g., nucleic acid molecules comprising ten nucleotides) is sufficient to anticipate an array containing any combination of nucleic acids, in a particular any 10-mer nucleic acid molecule.

In order to anticipate, a publication must "place the inventive compound or composition in the possession of the public" (Eli Lilly Co. v. Zenith Goldline Pharmaceuticals Inc., 471 F.3d 1369, 1375 (Fed. Cir. 2006)). The current claims cover microarrays containing oligonucleotides that include nucleic acid sequences having the listed mutations. Fodor describes a method for systematically producing arrays with every sequence of a given length. Fodor does not teach any single array that contains every sequence of any particular length. Rather, Fodor describes a

series of arrays designed in such way as to systematically include all possible nucleic acid sequences 10 nucleic acids in length. Because the total number of 10-mer sequences is so large, Fodor constructed four separate chips (Chips A-D, e.g., Figures 2-5), each including only a quarter of the total number of possible 10-mer sequences. Fodor does not provide any guidance as to which of the total possible sequences are on each chip. Therefore, no single chip taught by Fodor would necessarily anticipate the claimed microarrays, as Fodor does not teach a single chip with all of the claimed mutations.

Aside from the four chips actually produced by Fodor, the Examiner also argues that Fodor teaches construction of chips containing any conceivable sequence, including "all possible nucleic acid sequences of any given length."

Regarding anticipation, § 2131.02 of the M.P.E.P. states:

> If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be 'at once envisaged.' One may look to the preferred embodiments to determine which compounds can be anticipated. *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962).

While those skilled in the art at the time of filing might agree that Fodor teaches a method for making series of arrays encompassing every possible sequence of any given length, such a teaching would not have anticipated the current claims. Fodor does not teach any preferences for sequences with properties similar to oligonucleotides with the claimed mutations. Absent such a teaching, those skilled in the art at the time of the invention would not be in "possession" of the claimed microarrays, as the genus is too large for one skilled in the art to be able to "at once envisage" all of the individual species (See e.g., In Re Schaumann, 572 F.2d 312 at 316 (CAFC

1978) "In order to find anticipation in Petering, it was necessary to derive a class of compounds of lesser scope than the genus actually disclosed in the reference on the basis of preferences ascertainable from the remainder of the disclosure. . ."). Therefore, the rejection for anticipation should be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 10-12 are rejected as being obvious over Fodor in view of Kincaid (U.S. Patent Application Publication No. 2003/0186310). The Examiner argues that Kincaid teaches the use of fluorescently labeled control probes and that it would have been obvious to combine the control probes of Kincaid with the microarrays of Fodor. As stated above Fodor does not teach the claimed microarrays and Kincaid does not remedy this deficiency.

Furthermore, Kincaid discloses that "the control probe comprises a sequence of nucleic acids unique to the control probe" in the Abstract, whereas the quality control probes of present invention may have the same sequence as the target probes or arbitrary sequences as specified in claim 11. In addition, the control probe of Kincaid acts as a stilt essentially extending the oligomer test probe away from the surface of the microarray, whereas the quality control probes of the present claims do not extend the target probes, but rather are mixed with the target probes. The control probes of Kincaid also need control-specific target materials, after hybridization therewith a control signal indicative is interrogated, as described in Abstract, while the quality control probes of the present claims do not need any control-specific target materials and hybridization therewith. Therefore, Kincaid does not teach the claimed control probes and the rejection for obviousness should be withdrawn.

Claims 1-3 are rejected as obvious over Vernet et al. (Virus Research 82:65-71, 2002) in view of Liu et al. (Antiviral Chemistry and Chemotherapy 13:143-155, 2002). The Examiner argues that Vernet teaches the use of microarrays to diagnose HBV resistance to antibiotics. The Examiner states that Liu teaches the particular claimed mutations. In particular, the Examiner states that "Liu teaches that HBV pol genotypes E and G have drug resistant mutations at codon 529."

Liu describes codon numbering systems for various genotypes of HBV polymerase, which are not identical due to the differing N-termini of each of the genotypes. Liu provides a table showing an alignment of the sequences of the various genotypes that facilitates identification of the locations in each genotype corresponding to each of the identified mutations (page 146). In arguing that Liu taught all of the claimed mutations, the Examiner used the A genotype numbering system for demonstrating that Liu taught the 528 and 514 mutations of domain B and the 552, 548, and 555 mutations of domain C. Liu does not teach any mutation at the 529 codon of domain B using the A genotype codon numbering system. However, the Examiner maintained that using the alternate numbering system corresponding to the E and G genotypes of HBV pol, Liu teaches a mutation at codon 529.

The claims use the same numbering system for codons 528, 514, 552, 548, and 555 as they use for codon 529. This is made clear by the fact that the claims specify that the mutations are in "a HBV DNA polymerase gene." According to this numbering system, the codon 529 identified by the Examiner as containing a mutation actually corresponds to codon number 532, which is not specified as including a mutation in the present claims. Therefore, none of the references cited by the Examiner teach the claimed mutation in codon 529 of domain B. Because

none of the references alone, or in combination, teach each and every claim limitation, the rejection of claims 1-3 for obviousness should be withdrawn.

Claims 7 and 8 and claims 10-12 were rejected over Liu and Vernet in view of Anderson (U.S. Patent Application Publication No. 2003/0040870) and Kincaid (U.S. Application Publication No. 2003/0186310), respectively. Similar to Liu and Vernet, neither Anderson nor Kincaid teaches a probe against a mutation in codon 529. Therefore, neither Anderson nor Kincaid makes up for the deficiencies of Vernet and Liu in supporting an obviousness rejection of the present claims, as discussed above. The rejections of claims 7, 8, and 10-12 for obviousness should be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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